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I, KIM MARSHALL, MANAGER EXAMINATION SUPPORT AND SALES,
hereby certify that the annexed is a true copy of the Provisional specification in
connection with Application No. PO 7768 for a patent by CSL LIMITED filed on 9
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I further certify that the annexed specification is not, as yet, open to public
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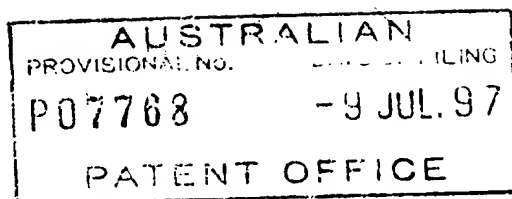
PRIORITY DOCUMENT



WITNESS my hand this Twentieth
day of July 1998

A handwritten signature in cursive script, appearing to read "Kim Marshall".

KIM MARSHALL
MANAGER EXAMINATION SUPPORT AND
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CSL Limited

A U S T R A L I A

Patents Act 1990

PROVISIONAL SPECIFICATION

for the invention entitled:

**"A METHOD OF ACHIEVING PRODUCTION GAINS IN LIVESTOCK AND
AGENTS USEFUL FOR SAME"**

The invention is described in the following statement:

- 1A -

A METHOD OF ACHIEVING PRODUCTION GAINS IN LIVESTOCK AND AGENTS USEFUL FOR SAME

The present invention relates generally to a method of achieving production gains in livestock and agents useful for same. More particularly, the present invention relates to a method of achieving production gains in pigs. The method of the present invention is useful for, *inter alia*, increasing the growth and/or decreasing the feed conversion ratio of livestock.

10 A declining demand for animal fat and an increasing demand for animal protein and lean meat has highlighted the need for the meat industry to consider the quality and quantity of meat produced. Of particular relevance to the issues of quality and quantity are factors such as:

- (i) the average daily gains in weight of livestock;
- 15 (ii) the feed consumed per kilogram of weight gain; and
- (iii) stress levels of livestock.

These factors are termed "production gains". In work leading up to the present invention, the inventors have developed a method for administering a lutenising hormone releasing hormone conjugate and slaughtering livestock animals which results in one or more of said production gains.

Accordingly, one aspect of the present invention relates to a method of achieving production gains in livestock said method comprising administering to said livestock an effective amount of lutenising hormone releasing hormone (LHRH)-conjugate at one or more spaced intervals prior to or about puberty and slaughtering said livestock at or about puberty.

Reference hereinafter to "LHRH" should be read as including reference to all forms of LHRH and derivatives thereof.

LHRH is by itself be too small to be antigenic, therefore conjugation to a carrier protein is required so that the LHRH which forms part of the LHRH-conjugate acts as a hapten and immunity is induced to LHRH. The carrier protein may be selected from a range of antigenic proteins available in a state of purity as described by Sad *et al* 1991.

5

The resulting LHRH-conjugate is administered to livestock as a preparation, which is referred to herein as a "composition", preferably by formulation in or with an adjuvant. The adjuvant is selected from the range of adjuvants known to induce high levels of antibody, including water in oil emulsions, oil in water emulsions, water in oil in water double
10 emulsions, saponin, Quill A extracts and other derivatives of saponin, DEAE-dextran, dextran sulphate, aluminium salts, nonionic block co-polymers and Iscoms. The adjuvant may include other immunomodulators, such as muramyl-dipeptide and derivatives, cytokines, and cell wall components from species of mycobacteria or corynebacteria. The adjuvant formulation may include a combination of two or more of the adjuvants listed. These lists are not to be taken
15 as exhaustive. The selection of adjuvant is in part dependant on the species being targeted and is based on the level and duration of the immune response required and on the lack of reactogenicity (ie tissue compatibility). The level of active component and adjuvant are chosen to achieve the desired level and duration of immune response.

20 Reference hereinafter to an LHRH-conjugate is not intended to be limited and should be read as including reference to all forms of LHRH or derivatives thereof, which are immunogenic.

"Derivatives" include fragments, parts, portions, chemical equivalents, mutants, homologs and analogs from natural, synthetic or recombinant sources, including fusion proteins.

25 For example, said LHRH includes peptides comprising a sequence of amino acids substantially as set forth in SEQ ID NO:1 or SEQ ID NO:2 or SEQ ID NO:3 or having at least 50% similarity thereto. The molecules defined in SEQ ID Nos:1, 2 and 3 are from the human. Chemical equivalents of LHRH can act as a functional analog of LHRH. Chemical equivalents may not necessarily be derived from LHRH but may share certain
30 similarities. Alternatively, chemical equivalents may be specifically designed to mimic certain physiochemical properties of LHRH. Chemical equivalents may be chemically

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synthesised or may be detected following, for example, natural product screening.

Homologs of LHRH contemplated herein include, but are not limited to, LHRH derived from different species.

5

"Derivatives" may also be derived from insertion, deletion or substitution of amino acids. Amino acid insertional derivatives include amino and/or carboxylic terminal fusions as well as intrasequence insertions of single or multiple amino acids. Insertional amino acids sequence variants are those in which one or more amino acid or non-natural amino acid residues are introduced into a predetermined site in the protein although random insertion is also possible with suitable screening of the resulting product. Deletional variants are characterised by the removal of one or more amino acids from sequence. Substitutional amino acid variants are those in which at least one residue in the sequence has been removed and a different natural or non-natural residue inserted in its place. Typical substitutions are those made in accordance with Table 1:

TABLE 1

Suitable residues for amino acid substitutions

	<u>Original Residue</u>	<u>Exemplary Substitutions</u>
20	Ala	Ser
	* Arg	Lys
	Asn	Gln; His
	Asp	Glu
	Cys	Ser
25	Gln	Asn
	* Glu	Ala
	* Gly	Pro
	* His	Asn; Gln
	Ile	Leu; Val
30	* Leu	Ile; Val

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	Lys	Arg; Gln; Glu
	Met	Leu; Ile
	Phe	Met; Leu; Tyr
	* Ser	Thr
5	Thr	Ser
	* Trp	Tyr
	* Tyr	Trp; Phe
	Val	Ile; Leu
10	Key: Amino acid residues marked with an asterisk indicate residues present in the human LHRH sequence.	

Examples of non-natural amino acids include, but are not limited to the D-isomers of said amino acids. "Additions" to amino acid sequences include fusion with other peptides, polypeptides or proteins.

15

The LHRH-conjugate may be administered to the livestock in a single-dose, for example a single administration of a pulsatile release vaccine or in multiple doses. Preferably said LHRH is administered at two spaced intervals.

20 Accordingly there is provided a method of achieving production gains in livestock said method comprising administering to said livestock an effective amount of LHRH-conjugate at two spaced intervals prior to or about puberty and slaughtering said livestock at or about puberty.

25 In a most preferred embodiment, said LHRH comprises the amino acid sequence substantially as set forth in SEQ ID NO:2 and wherein the carboxyl terminus of said amino acid sequence is amidated. Said preferred LHRH is referred to herein as "LHRH 2-10 form".

Accordingly, there is provided a method of achieving production gains in livestock said
30 method comprising administering to said livestock an effective amount of an LHRH 2-10 form-conjugate at one or more spaced intervals prior to or about puberty and slaughtering

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said livestock at or about puberty.

Even more preferably said LHRH 2-10 form-conjugate is administered at two spaced intervals.

5

According to this most preferred embodiment there is provided the method of achieving production gains in livestock said method comprising administering to said livestock an effective amount of an LHRH 2-10 form-conjugate at two spaced intervals prior to or about puberty and slaughtering said livestock at or about puberty.

10

Slaughtering of said livestock "at or about puberty" should be understood to include slaughtering livestock up to 10 weeks post-puberty.

The term "production gains" includes but is not limited to an increase in final weight of
15 said livestock at slaughter, a lower feed requirement for each kilogram of carcass weight gained, a faster growth rate of said livestock as compared to untreated livestock or decreases in stress levels of livestock.

The term "livestock" includes but is not limited to mammals such as pigs, cattle, sheep;
20 captive wild animals such as deer; and aves such as emus or ostriches. Most preferably, said livestock are pigs. Even more preferably said pigs are male.

According to this most preferred embodiment, there is provided a method of achieving production gains in male pigs said method comprising administering to said male pigs an
25 effective amount of an LHRH 2-10 form-conjugate at two spaced intervals prior to or about puberty and slaughtering said male pigs at or about puberty.

To achieve these production gains in pigs, the composition must be administered at a critical time in the growing phase of the pigs. The composition is preferably administered
30 as two injections, separated by a suitable time interval. The effective level and duration

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of antibody is not induced until after the second administration of composition. Giving the second administration of composition too early results in effective castration at a critical stage of growth and would result in poor feed conversion, higher fat content of the carcass and slower weight gain. Giving the second administration of composition too late, i.e. too close to slaughter, would result in a tainted carcass and too little time for the modifying effect on behaviour for the production gains to be realised.

Preferably, the first administration of an LHRH 2-10 form-conjugate to the male pig is at 8 to 18 weeks of age, the second administration of an LHRH 2-10 form-conjugate is at 4 to 6 weeks prior to slaughter and said pig is slaughtered at 24 to 26 weeks of age. Even more preferably, the first administration is at 18 weeks of age, the second administration is at 22 weeks of age and said pig is slaughtered at 26 weeks of age.

Another aspect of the present invention relates to a preparation for use in achieving production gains in livestock comprising an LHRH-conjugate formulated in or with an adjuvant.

Although not intending to limit the invention to any one method, said peptide may be synthesised by Fmoc chemistry and the resulting peptide coupled to a carrier protein. Said coupling may be performed as described in Ladd *et al* 1990 or in Bonneau *et al* 1994, and the resulting conjugate of peptide and carrier protein (referred to herein as "peptide-conjugate") processed to be free of unbound peptide and other biproducts of conjugation. Such processing may be achieved by conventional dialysis or by ultrafiltration. The resulting peptide-conjugate may be formulated in or with an adjuvant, for example adsorbed to an adjuvant, as hereinbefore described.

Preferably, said LHRH is the LHRH 2-10 form. More preferably, said LHRH 2-10 form is conjugated to diptheria toxoid.

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Accordingly, there is provided a preparation for use in achieving production gains in livestock comprising an LHRH 2-10 form peptide conjugated to diptheria toxoid, said peptide-conjugate being adsorbed to adjuvant.

5 Even more preferably, said adjuvant is DEAE-Dextran.

According to this most preferred embodiment there is provided a preparation for use in achieving production gains in livestock comprising an LHRH 2-10 form peptide conjugated to diptheria toxoid, said peptide-conjugate being adsorbed to DEAE-Dextran.

10

Yet another aspect of the present invention contemplates a veterinary composition comprising an LHRH-conjugate adsorbed to an adjuvant.

Preferably said LHRH-conjugate is the LHRH 2-10 form conjugated to diptheria toxoid
15 and most preferably said LHRH 2-10 form-diptheria toxoid conjugate is adsorbed to DEAE-Dextran.

Accordingly, there is provided a veterinary composition comprising an LHRH 2-10 form conjugated to diptheria toxoid said LHRH 2-10 form-diptheria toxoid conjugate being
20 adsorbed to DEAE-Dextran.

The veterinary forms suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. It must be stable under the conditions of manufacture and
25 storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol and liquid polyethylene glycol, and the like), suitable mixtures thereof, and vegetable oils. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the
30 maintenance of the required particle size in the case of dispersion and by the use of surfactants. The prevention of the action of microorganisms can be brought about by various

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antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example,
5 aluminum monostearate and gelatin.

Sterile injectable solutions are prepared by incorporating the active compounds in the required amount in the appropriate solvent with various of the other ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by
10 incorporating the various sterilized active ingredients into a sterile vehicle which contains the basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and the freeze-drying technique which yield a powder of the active ingredients plus any additional desired ingredient from previously
15 sterile-filtered solution thereof.

When the active ingredients are suitably protected they may be orally administered, for example, with an inert diluent or with an assimilable edible carrier, or they may be enclosed in hard or soft shell gelatin capsule, or compressed into tablets, or incorporated directly with
20 the food of the diet. For oral administration, the active compound may be incorporated with excipients and used in the form of ingestible tablets, buccal tablets, troches, capsules, elixirs, suspensions, syrups, wafers, and the like. Such compositions and preparations should contain at least 1% by weight of active compound. The percentage of the compositions and preparations may, of course, be varied and may conveniently be between about 5 to about
25 80% of the weight of the unit. The amount of active compound in such useful compositions is such that a suitable dosage will be obtained. Preferred compositions or preparations according to the present invention are prepared so that an oral dosage unit form contains between about 0.1 μ g and 2000 mg of active compound.

30 The tablets, troches, pills, capsules and the like may also contain the components as listed hereafter: A binder such as gum, acacia, corn starch or gelatin; excipients such as dicalcium

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- phosphate; a disintegrating agent such as corn starch, potato starch, alginic acid and the like; and a lubricant such as magnesium stearate. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. A
- 5 syrup or elixir may contain the active compound, methyl and propylparabens as preservatives, and a dye. Of course, any material used in preparing any dosage unit form should be veterinarily pure and substantially non-toxic in the amounts employed. In addition, the active compound(s) may be incorporated into sustained-release preparations and formulations.
- 10 Veterinarily acceptable carriers and/or diluents include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents and the like. The use of such media and agents for veterinarily active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, use thereof in the therapeutic compositions is contemplated. Supplementary active
- 15 ingredients can also be incorporated into the compositions.

- It is especially advantageous to formulate parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. For administration to livestock it is particularly advantageous to use a multi-dose container linked to a repeating vaccination gun.
- 20 Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subjects to be treated; each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the novel dosage unit forms of the invention are dictated by and directly dependent on (a) the unique characteristics of the active material and
- 25 the particular therapeutic effect to be achieved, and (b) the limitations inherent in the art of compounding such an active material for the treatment of disease in living subjects having a diseased condition in which bodily health is impaired as herein disclosed in detail.

- The principal active ingredient is compounded for convenient and effective administration in
- 30 effective amounts with a suitable veterinarily acceptable carrier in dosage unit form as hereinbefore disclosed. A unit dosage form can, for example, contain the principal active

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compound in amounts ranging from 0.5 µg to about 2000 mg. Expressed in proportions, the active compound is generally present in from about 0.5 µg to about 2000 mg/ml of carrier. In the case of compositions containing supplementary active ingredients, the dosages are determined by reference to the usual dose and manner of administration of the said
5 ingredients.

Further features of the present invention are more fully described in the following Examples. It is to be understood, however, that this detailed description is included solely for the purposes of exemplifying the present invention. It should not be understood in any
10 way as a restriction on the broad description of the invention as set out above.

EXAMPLE 1

PREPARATION OF LHRH-CONJUGATE COMPOSITION

15 The LHRH-conjugate is based on a synthetic 2-10 form of Lutenising Hormone Releasing Hormone (LHRH) peptide coupled to a carrier protein. The peptide by itself is too small to be antigenic, and coupling to a carrier protein is required so that the peptide acts as a hapten and immunity is induced to LHRH. The carrier protein may be selected from a range of antigenic proteins available in a state of purity as described by Sad et al, 1991.

20

The peptide is synthesised by Fmoc chemistry and the resulting 2-10 form LHRH peptide is coupled to carrier protein. The coupling may be performed as described in Ladd et al. 1990 or in Bonneau et al. 1994, and the resulting conjugate of peptide and carrier protein processed to be free of unbound peptide and other by-products of conjugation. Such processing may
25 be achieved by conventional dialysis or by ultrafiltration.

The resulting conjugate may be used to prepare a composition for administration by formulation with or in an adjuvant. The adjuvant is selected from the range of adjuvants known to induce high levels of antibody, including water in oil emulsions, oil in water
30 emulsions, water in oil in water double emulsions, saponin, Quill A extracts and other derivatives of saponin, DEAE-dextran, dextran sulphate, aluminium salts, nonionic block co-

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polymers and Iscoms. The adjuvant may include other immunomodulators, such as muramyl-dipeptide and derivatives, cytokines, and cell wall components from species of mycobacteria or corynebacteria. The adjuvant formulation may include a combination of two or more of the adjuvants listed. These lists are not to be taken as exhaustive. The selection of adjuvant is in part dependant on the species being targeted and is based on the level and duration of the immune response required and on the lack of reactogenicity (ie tissue compatibility). The level of active component and adjuvant are chosen to achieve the desired level and duration of immune response.

10

EXAMPLE 2**APPLICATION OF PRODUCTION GAIN PROTOCOL TO PIGS**

A composition comprising LHRH conjugated to diptheria toxoid and adsorbed to DEAE-dextran was administered by injection to 50 male pigs. A second group of 50 male pigs acted as placebo administered controls and 50 additional pigs were castrated prior to weaning.

The pigs were divided into 3 groups each of 50 animals. Groups were housed in adjacent pens and fed the same diet.

20 Group 1. LHRH conjugate composition administered by injection at 18 and 22 weeks of age, and slaughtered at 26 weeks.

Group 2. Placebo (adjuvant plus unconjugated diptheria toxoid administered by injection) at 18 and 22 weeks of age, and slaughtered at 26 weeks.

25

Group 3. Castrated at 2-3 weeks of age, untreated, and slaughtered at 26 weeks.

The pigs were housed indoors in pens on concrete and slated floor, with pelletised feed provided *ad-libitum* at one end of the pen and bite-drinkers and slatted dunging area at the other. The trial was conducted blind.

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All pigs were weighed at the start of the experiment (18 weeks of age) and every 2 weeks thereafter. The final live weight was determined at slaughter at 26 weeks of age.

Feed consumption per pen was monitored from the time of the booster administration.

5

Serum samples were taken at 2 and 4 weeks post administration for the analysis of antibody responses to LHRH.

EXAMPLE 3

10

RESULTS OF PRODUCTION GAIN PROTOCOL

Antibody responses were induced in all recipients of the LHRH-conjugate composition and no antibody titres were detected in control pigs. Table 2 shows anti-LHRH titres in recipients of composition 2 and 4 weeks after the second administration of LHRH-conjugate
15 composition.

Table 2. Anti - LHRH titres induced by administration of LHRH-conjugate composition.

20

	TITRE
MEDIAN TITRE 2 WEEKS POST BOOST	1077
TITRE RANGE AT 2 WEEKS	248-11681
MEDIAN TITRE AT 4 WEEKS POST BOOST	478
25 TITRE RANGE AT 4 WEEKS	103-1532

These titres demonstrate that all pigs responded with a strong antibody response at 2 weeks post second administration of the LHRH-conjugate composition and that there was a general decline in the antibody titres over the next 2 weeks prior to slaughter.

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Production parameters measured in this trial were the feed used and the weight of each pig at fortnightly intervals after second administration of LHRH-conjugate composition. The weights of individual pigs allowed calculation of average daily weight gains. The results are shown in Table 3.

5

Table 3. Live weight(kg) from the time of second administration of LHRH-conjugate composition to slaughter and average daily weight gains (gm).

10		LHRH- CONJUGATE COMPOSITION TREATED PIGS	UNTREATED PIGS	CASTRATES
	WEIGHT AT BOOST	88.8	89.3	93.4
	WEIGHT PRE- SLAUGHTER	120.7	113.3	117.1
15	AVERAGE DAILY GAIN OVER LAST 4 WEEKS	1119.3	858.4	846.7

Pigs were penned in groups of 10 and thus each group of 50 pigs was housed in 5 pens.

20 Feed usage was monitored on a pen basis and the usage averaged over the number of pigs in the pen. Combination of feed usage with weight gain enabled the calculation of feed conversion ratios ie the weight of feed consumed per pig for each kg of carcase weight gained.

25

Table 4. Feed used per pen over the 4 weeks (kg) after second administration of LHRH-conjugate composition and the feed conversion ratio (kg feed consumed to kg live weight gain)

5		LHRH- CONJUGATE COMPOSITION TREATED PIGS	UNTREATED PIGS	CASTRATES
	FEED USED	890.8	766.4	841.6
	FEED CONVERSION RATIO	3.099	3.299	3.739

10

LHRH-conjugate composition treated pigs show improvement over normal entire pigs in improved average daily gain, final live pre-slaughter weights and lower, ie improved feed conversion ratios.

- 15 Scoring of carcasses on the slaughter chain for those carcasses showing marked signs of fighting is shown below. There was a significant decrease in the degree of fighting of LHRH-conjugate composition treated pigs. Refer to Table 5. This decrease in fighting will result in a lower level of stress for LHRH-conjugate composition treated pigs and should therefore improve the quality of meat. Fighting is exacerbated during transport and
- 20 lairage at the abbatoir prior to slaughter, and includes significant stress levels. These stress levels have been shown to alter the final pH and water retention properties of meat, affecting quality parameters of colour and texture.

Table 5. Fighting scores of carcasses after slaughter.

GROUP	NUMBER SCORED AS FIGHTING
5 LHRH-CONJUGATE COMPOSITION TREATED PIGS	4
UNTREATED PIGS	26

Those skilled in the art will appreciate that the invention described herein is susceptible to
 10 variations and modifications other than those specifically described. It is to be understood
 that the invention includes all such variations and modifications. The invention also
 includes all of the steps, features, compositions and compounds referred to or indicated in
 this specification, individually or collectively, and any and all combinations of any two or
 more of said steps or features.

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SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: CSL LIMITED

(ii) TITLE OF INVENTION: A METHOD OF ACHIEVING PRODUCTION
GAINS IN LIVESTOCK AND AGENTS USEFUL
FOR SAME

(iii) NUMBER OF SEQUENCES: 3

(iv) CORRESPONDENCE ADDRESS:

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(E) COUNTRY: AUSTRALIA
(F) ZIP: 3000

(v) COMPUTER READABLE FORM:

(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.25

(vi) CURRENT APPLICATION DATA:

(A) APPLICATION NUMBER: AU PROVISIONAL
(B) FILING DATE: 01-JAN-1996
(C) CLASSIFICATION:

(viii) ATTORNEY/AGENT INFORMATION:

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(2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

Glu His Trp Ser Tyr Gly Leu Arg Pro Gly
 5 10

(2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 9 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

His Trp Ser Tyr Gly Leu Arg Pro Gly
 5

(2) INFORMATION FOR SEQ ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 8 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Trp Ser Tyr Gly Leu Arg Pro Gly
 5

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Dated this 9th day of July, 1997.

CSL Limited
by its Patent Attorneys
DAVIES COLLISON CAVE